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Translating a sub-Saharan African countries' experience in Human papillomavirus vaccination to a single dose regimen.

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Translating a sub-Saharan African countries' experience in Human papillomavirus vaccination to a single dose regimen.

Directed by Professor Myung Ken Lee

A Master's Thesis
Submitted to the Department of Global Health Security
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and the Graduate School of Public Health of Yonsei University
in partial fulfillment of the
requirements for the degree of
Master of Public Health.

Onesmo Daimon Mwegoha

December 2019

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List of Abbreviation

AEFI	Adverse Effect Follow Immunization
DNA	Deoxyribonucleic acid.
EPI	Expanded Program on Immunization.
FDA	Food and Drug Authority.
GAP	Gardasil Access Program.
GAVI	GAVI The Vaccine Alliance.
GNI	Gross National Income.
HPV	Human Papillomavirus.
LMIC	Lower Middle-Income Countries.
NBS	National Bureau of Statistics
NPI	National Program of Immunization.
NVS	New Vaccine Support.
PATH	Program for Appropriate Technology in Health.
SA	South Africa
SSA	Sub-Saharan Africa.
UNICEF	United Nations International Children's Education Fund
US	The United States.
VA	Vaccine Adherence

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VUR Vaccine Uptake Rate

WHO World Health Organization.

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Definition of Keywords.

Cancer of Cervix	A slow-growing malignant tumor originating from the cervix commonly caused by the human papillomavirus.
Demonstration Project	Initiation of a live project by a person or organization with a primary objective of promoting innovation and obtain the best practice on how the future or scaling up should be done.
Vaccine Introduction	A process of inserting a new vaccine into the national immunization program.
Immunogenicity	The ability of a substance or antigen to provoke the development of adequate immunity against a similar antigen or substance in the future encounter.
Drug resistance	The ability of microorganisms to grow or survive in the presence of a drug (either antimicrobial or anticancer) at a concentration that was previously sufficient to inhibit or kill them.
Financial cost	Actual or direct expenditure incurred when executing a vaccination program usually reported in a normal accountant report.
Economical cost	Are all costs not covered in financial cost and monetized values.

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Abstract

Background: Human Papilloma Virus (HPV) is a sexually transmitted virus that is known to cause different types of cancer including cancer of the cervix. Cancer of cervix is common among women and most of the burden is from SSA countries. Moreover, most of these countries are not yet having HPV vaccination programs while low coverage is seen in some few countries which already had the programs.

WHO recommends two doses of the HPV vaccine are effective to prevent girls against the HPV infection. However, there are many studies currently being conducted to prove the effectiveness of a single-dose regimen.

Objectives: The aim of this study is to identify the most common lessons learned in the HPV programs in SSA countries and conduct the budget impact analysis of a single dose regimen for HPV vaccination in Tanzania as a way to determine the future cost.

Methods: This is mixed-method study with a qualitative part covers a literature review of both published and unpublished documents, and reports of HPV demonstration programs from SSA countries while the quantitative part involves budget impact analysis by using secondary data.

Published documents were obtained from PubMedicine while unpublished documents were obtained from the WHO website, HPV Information Centre as well as the websites of the ministry of health of respective countries.

Results: 22 key lessons were reported in seven specific focus areas which included national policy and planning, service delivery, workforce, linkage with other interventions, monitoring and evaluation, financial support, and sustainability and scale-up. We also found out that there

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were similar lessons across eight SSA countries that had finished the HPV demonstration project however, there was a variation of the strength of the lessons.

The economic and financial cost for HPV vaccination in Tanzania was determined and it was estimated that country could save about 5,927,820.57 USD per year on an average from the year 2015 to 2020 as an economic cost if single-dose regimen was to be used.

Conclusion: SSA countries with no experience in the HPV vaccination program and those with reported low coverage should take advantage of studying best practices from other SSA countries. Also, although still there is no enough evidence for the single-dose regime of HPV vaccination, SSA countries should be prepared to move to a single dose regimen once evidence is gathered as it would reduce the budgetary burden.

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1. **INTRODUCTION**.

1.1 Background

Cancer of the cervix is one of the cancers that is known to be caused by a viral infection. It is reported that human papillomavirus (HPV) causes nearly all cervical cancers and some cancers of the vagina, vulva, penis, anus, and oropharynx (Shiels et al. 2015). In SSA the burden of cancer of the cervix has been increasing gradually in recent years owing to several factors and according to the World Health Organization, cervical cancer will kill more than 443,000 women per year worldwide by 2030, about 90 % of them in SSA (WorldCancerResearchFund 2019).

Cervical cancer is the fourth most common cancer among women and eighth among commonly occurring cancer overall (Mboumba Bouassa et al. 2017). The situation is far most worse among developing countries whereby all ten countries with the highest burden of cervical cancer are from sub-Saharan Africa (WorldCancerResearchFund 2019). In addition, the burden of cancer of the cervix is not equally shared among the regions in SSA. Some of the regions have a bigger burden compare to others. It was reported by International Agency for Research on Cancer (IARC) in 2012 that age-standardized incidence and mortality rates due to cancer of cervix are highest in Eastern Africa, which also has the highest HPV prevalence in the general population (20.5% compared with 18.6% which is overall HPV incidence in SSA and 4.1% which is global prevalence).

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Human Papilloma Virus, HPV is a sexually transmitted DNA virus that is known to cause different types of cancers. Since it's discovery in 1956, many subtypes have been isolated and been associated with different cancers and other diseases. Despite its lethal sequel; the infection is so common that sexually active men and women are susceptible to acquiring genital HPV infection. The life-time risk of HPV infection is up to 80% (Panatto et al. 2012). However, most HPV infections are asymptomatic and clear spontaneously within 1 to 2 years; although persistent infection with oncogenic HPV types can lead to the development of pre-cancer or cancer (Schiffman et al. 2007).

The common HPV subtypes that are involved in cervical cancer include; 6, 11, 16, 18, 31, 33, 45, 52, and 58. Among these, HPV subtypes 16 and 18 are referred to as highly oncogenic subtypes responsible for about 7.7% of all cancers in developing countries, mainly cervical cancer (Rodriguez et al. 2008).

Cervical cancer can be prevented primarily by vaccination as well as secondarily through screening women at risk. Usually, the vaccine will prevent the vaccine from HPV infection which is the causative agent while the early screen is a mean to prevent the development of cancer from precancerous lesions. There are mainly three vaccines that are available in the market for the prevention of cervical cancer. One is Cervarix, a bivalent vaccine that averts the infection from HPV subtypes 16 and 18, while quadrivalent vaccine Gardasil prevents an individual from all cancers caused by subtypes 6, 11, 16 and 18.

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In addition, already a nonavalent vaccine (Gardasil 9) is in the market and some developed countries like Australia already are using it in its vaccination program which prevents the infection from nine HPV subtypes. Gardasil 9 was approved by America FDA in 2014 and replaced quadrivalent Gardasil in HPV vaccination programs in the US (The U.S. Food and Drug Administration 2018).

WHO recommends two doses of HPV vaccine which should be at least 6-12 months apart from young girls aged between 9-14 years old for acquiring adequate immunogenicity. Also, three doses are recommended for young girls older than 14 years old and those who are immunocompromised. For Gardasil 9, in 2014 U.S FDA recommends the age from 9 to 26 and later in 2018 expanded the age coverage from 27 to 45 (The U.S. Food and Drug Administration 2018). Moreover, several studies are currently being conducted to establish the effectiveness of a one-dose HPV vaccine. If the effectiveness shall be established many countries particularly those with little experience in the area of HPV vaccination shall benefit in several ways.

The secondary prevention of cancer of the cervix can be achieved by screening women at risk and treat accordingly when the early symptoms are present. For an effective reduction of the burden of cervical cancer, it is important that HPV vaccination and cervical cancer screening go simultaneously.

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One of the ways to reduce the burden of the cancer of the cervix in SSA is by vaccinating young girls as recommended by WHO in as many countries as possible. However, to introduce the HPV vaccination on a nation-wide scale in a more cost-effective way and achieving maximum coverage conducting a demonstration project and learning from other countries is essential. To narrow down the areas of focus during the demonstration project for the countries which are beginning the process, documenting the lessons learned and sharing them with other countries is a stepping stone.

Currently, many SSA countries are still conducting the demonstration project and few had completed the project and introduce the vaccine in EPI. To launch any new vaccine program, there should be an adequate fund to cover both financial and economic costs. This has always been a limiting factor for the integration of new vaccines in EPI among many developing countries particularly SSA countries. To overcome this; the international organization such as GAVI provide support for those countries which are to introduce the new vaccine in their NPI. This is called New Vaccine Support NVS and usually depends on the recipient country's GNI per capita.

Countries become eligible for Gavi's support if their average Gross National Income (GNI) per capita has is less than or equal to US$ 1,580 over the past three years (according to World Bank data published in July each year). Once a country crosses the eligibility threshold, it

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enters the accelerated transition phase and starts to phase out of our financial support (GAVI 2019).

Conducting a demonstration project is the first step towards the country's introduction of the vaccine as it provides a rough picture of how the program is going to be and therefore strengthen preparedness as well as provide a way to avoid some fatal mistakes which would cost the program greatly. Also, the lessons learned from these demonstration projects in one country can be used as a guide for other countries with similar characteristics that have not yet integrate HPV vaccination in routine vaccines or modify the HPV vaccination nation-wide project. The demonstration project shall not be confused with a pilot or introduction of the vaccine. The pilot is an initial rollout of the project which commonly has some limited scope. Usually, the limited scope can be in terms of a number of users or the area coverage.

Most SSA countries that conducted demonstrations took a relatively long time from demonstration to the nation-wide vaccination program to the entire country as compare to developed countries. Reasons being financial constraints and technical issues. Few had successfully conducted the demonstration and the already HPV vaccine is integrated into national EPI. By May 2018, only seven African countries (Libya, Uganda, Seychelles, Rwanda, South Africa, Botswana, and Lesotho) had an HPV vaccination program at a national level (Chido-Amajuoyi et al. 2019). However, according to PATH, only seven SSA countries will be having an HPV vaccination program national wide by the end of 2019.

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1.2 Rationale

In spite of statistics proposing that the largest proportion of cervical cancer burden both current and projected one is coming from SSA countries, few of them had shown adequate effort on reducing this burden by introducing HPV vaccine nationwide. Many studies have been conducted to offer a guideline towards the introduction of the HPV vaccine in LMIC in general.

These studies do not offer a distinctive way forward among SSA countries as LMIC consist of countries from different parts of the world with different culture and traditions which all are the determinants of the health-seeking behavior. What works in LMIC in Asia could not work in LMIC in SSA, therefore having more localized lessons for the SSA countries could help in speeding up the launching of HPV vaccination projects in these countries. There is a considerable small number of studies that have been conducted to provide some valuable lessons that can be beneficial to other SSA countries.

This study intended to summarize the most common lessons learned in HPV demonstration projects among SSA countries that either already have HPV vaccination in the national EPI or had successfully completed the HPV vaccine demonstration in their countries. Also, the study aimed to show other descriptive such as coverage achieved and time used in the demonstration with respect to the approach that was used to show the best practice.

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We anticipate that this study shall facilitate other SSA countries that have not yet started the implementation of HPV vaccination to design a more cost-effective program by concentrating on the lessons provided on the results of this study.

1.3 Hypothesis.

In this study, our assumption is that "there are more similarities in recommendations from demonstration projects conducted in SSA countries as compare to studies that combined LMIC from different continents".

According to Russel M et al. 2013, it was suggested that there may not be a "gold standard" vaccination program applicable on a global or even national scale. Rather, tailoring vaccine campaigns to meet the needs, challenges, and cultural priorities of specific regions or communities appear to generate programs with a high rate of success. This means the previous studies which summarize the situation in LMIC could not reflect the real situation in some SSA countries and therefore review the lessons specifically for the SSA could provide a more similarity of the lessons compared to those of LIMC.

1.4 Goal and Objectives

The goal of this study was to provide a recommended plan on how to conduct the HPV vaccination program in a more cost-effective way. As many studies had previously been conducted to provide some lessons and compared the VUR among countries that are

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geographically not the same so as to determine what it is important when an HPV vaccination is being conducted. However many studies have provided the recommendation based on the findings from LMIC which might not be the case for the SSA countries.

Also in this study, we identified the country-specific the most common lessons learned during the HPV programs among SSA countries aiming to provide the best practice to the countries which are either not yet conducting the program or are having the low coverage of the vaccination by doses.

We also compared the coverage of HPV vaccines by doses among few SSA countries so as to provide a great value of the lessons identified from those specific countries. As reported by Ladner et al. 2014 the coverage (VUR) is being determined by multiple factors, therefore lessons from the countries with high coverage may be of great contribution to other countries.

This study also determined the factors contributing to partial or no vaccination. No vaccination means; the presence of the individual who falls into target population but ends up being not vaccinated at the end of the program while partial vaccination refers to the situation whereby an individual is having fewer doses as compared to the recommended one. Usually all program does not meet their expected target. This can be due to no refusal or partial vaccination as it had been reported by Watson-Jones et al. 2015. This study reviewed reports

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from other HPV programs conducted in SSA countries to determine the factors that are affecting the partial and no vaccination.

In addition, this study determined a budget impact analysis of a single dose regimen of the HPV vaccine in Tanzania. This will help to estimate the overall budgetary burden reduction if the effectiveness of the single-dose regimen is going to be established. We chose Tanzania as case for budget impact analysis.

2. LITERATURE REVIEW

A demonstration project is a means of promoting innovations and capturing and disseminating best practices through the development and analysis of a live project. The demonstration project is used to provide a proof of concept for the intended project. A proof of concept is a realization of certain methods or ideas.

Usually, when conducting a demonstration project the primary outcome is to carry out a pilot program that includes some form of research that contributes to a program change and/or policy-making for a new program. In many cases demonstration is anticipated to provide scientific evidence of the best practice so as to create a more cost-effective program. For this reason, the demonstration project is usually taking place in the areas with almost similar natural environments with the area where the real project is going to be conducted.

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Follow the licensure of the first HPV vaccine the USA was the first country to introduce the vaccine among girls in 2006, then in 2011 it moved to a gender-neutral HPV vaccination and it was the first country to do so as well (Markowitz et al. 2018). Many developed countries also joined by providing HPV vaccine to young girls. However, the use of the vaccine in most LMIC has not been enormously adopted particularly in SSA countries.

The past 10 years have seen remarkable progress in the global scale-up of human papillomavirus (HPV) vaccinations and most of these have occurred in the last 4 years (LaMontagne et al. 2017). Despite the increased endorsement of this vaccine among LLMIC few countries particularly in SSA have introduced the vaccine country-wide. According to Grahan et al 2011; the three major reasons that prohibit delivering vaccines in marginalized women include the high cost of the vaccine, the absence of delivering infrastructures and inadequate community participation in creating awareness of the importance of HPV vaccine among vaccinee.

Many studies had been studied the best practice for the HPV vaccine demonstration project by compiling the lessons learned from different parts of the world. Most of these had assumed the similarities among LMIC and therefore the best practice for HPV demonstration has been made for LMIC.

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One of the recent studies that were published in 2017 by N Howard reviewed the lessons learned in 45 LMIC to see what can be the appropriate approach when implementing the HPV introduction in any LMIC (Howard et al. 2017). This was a mixed-method study that involved a systematic literature review and key informant interview. The articles involved in this study were both published and unpublished one as well as reports of HPV pilot/demonstration projects from the ministry of health of the respective country. Also, the study included a key informant interviewee in which about 56 of them participated. Furthermore, there were 61 reviewed peer articles, 11 conference abstracts, and 188 technical reports. Generally, there was information from about 66 demonstrations from different LMIC countries.

This is the strength of the study as it had a wide range source of data, however, for the same reason this might have resulted in a generalization of what can work in different countries due to scatteredness of sources of data. Although LLMIC has almost similar problems, variations still do exist. According to report by WHO on ten health threats on global health 2019; the world is facing multiple health challenges and these range from outbreaks of vaccine-preventable diseases like measles and diphtheria, increasing reports of drug-resistant pathogens, growing rates of obesity and physical inactivity to the health impacts of environmental pollution and climate change and multiple humanitarian crises (World Health Organization 2019). Most of these threats are shared in LLMIC and in the place where there is a big number of displaced people like Myanmar it is clear different policies and strategies are

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needed to address the same problem as compare to Namibia where some societies are still living in an isolated area.

Also in this study, the author did not provide adequate information in some of the important areas required for immunization coverage and equity. According to GAVI, there are six strategic focus areas in immunization which include; immunization supply chains, data quality, availability and use, in-country leadership, management and coordination, demand promotion, in-country political will and financial and programmatic sustainability (Gavi The Vaccine Alliance 2017). The author did not mention anything about data management which is important for the monitoring and evaluation of the project. Also, the area of the supply chain was not clear for issues like the cold chain and vaccine delivery to a hard to reach areas.

According to a report published by PATH 2018, many LMIC particularly those form SSA have been conducting an HPV demonstration project, however many had been on-hold of the program for several years before resuming and complete the project. This study also did not address the reason why many projects have been wasting time by stopping several years regardless of adequate planning.

The other study which explained about lessons learned in HPV vaccination was conducted between 2009 and 2013 by Joel Ladner and others. This study was conducted in LMIC by the help of Merck & Co under the program call Gardasil access program, GAP whereby 21 projects

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from 14 LMIC received vaccine for implementation of the project so that to gain operational experience designing and implementing HPV vaccination programs, with the goal of supporting the development of successful child and adolescent immunization models (Ladner et al. 2014).

During this program local and national institutes, as well as organizations, were the main designers and implementers, the goal was to gain experience in the development of relevant and effective strategies for addressing issues that can affect coverage rates, such as infrastructure, culture, and politics among participating institutes and organizations (Ladner et al. 2014). The organizations were obligated to cover other costs of vaccination such as delivery and cold chain.

The projects were divided in terms of delivery strategy in that; 12 programs were school-based, five were health clinic-based, and four programs were mixed models (Ladner et al. 2014). The delivery mode was identified by mode by which more than 80% of the targeted population were vaccinated by. A mixed model was when both school-based and health clinic delivery strategy was used and none of the delivery strategies vaccinated more than 80% of the targeted population. In this study, the effectiveness of the project was assessed by vaccine uptake rate VUR and vaccine adherence VA. VUR was defined as the number of vaccinated girls that received a full course of vaccination (three doses) divided by the number of girls

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targeted while VA was defined as the number of girls receiving a full course of vaccination divided by the number of girls who received a first dose (Ladner et al. 2014).

3. **METHOD**.

This study took a mixed method by combining both qualitative and quantitative approaches. It involved a literature review of both published, unpublished articles, reports of HPV demonstration projects and other articles explaining lessons learned in HPV vaccination programs from SSA countries which either had already rolled out a national HPV vaccination program or successfully conducted its HPV demonstration project.

The qualitative part is between a case study type-narrative study and it covers the lessons learned from different SSA countries during the HPV vaccine program and other studies that cover lessons learned during HPV vaccination programs. Also, the same or different studies were also involved to determine the factors that can influence partial or no HPV vaccination among the target population. Lessons from different published articles and reports were summarized in the excel sheet and analyzed by using deductive and inductive coding thematic analysis. The strength of the individual lesson in this accord was determined by the frequency in which a particular lesson had appeared in different articles or reports.

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The SSA countries that had rolled out a nationwide HPV vaccination program or successfully conducted an HPV demonstration project by June 31, 2019 were identified by concurrent triangulation of two sources which are; “Projected and current national introductions, demonstration/pilot projects, gender-neutral vaccination programs, and global HPV vaccine introduction maps”, published from PATH and compared to Human Papillomavirus and Related Diseases Report African region (HPV information centre 2019). The countries identified were; Botswana, Lesotho, Mauritius, Mozambique, Rwanda, Senegal, Seychelles, South Africa, Tanzania and Uganda.

Those studies and report which did not articulate the lessons learned from the HPV vaccination demonstration more not involved in this review. Also, the review did not include all SSA countries which are currently conducting HPV demonstration. Several keywords were used to obtain these articles and reports which included; Human papillomavirus HPV, vaccine, demonstration, introduction, campaign and SSA.

On the other hand; the quantitative part of the study involved comparing vaccination coverage among SSA countries and budget impact analysis of the HPV vaccine from two doses to a single dose regimen in Tanzania. Data for comparison of the coverage of HPV vaccination among different SSA countries were obtained from different articles form PubMedicine and reports.

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We used secondary data from Gavi and UNICEF for vaccine price, financial and economic cost for the budget impact analysis of the single-dose regimen in Tanzania. The estimated number of the total target population was obtained from as well as Tanzania National Bureau of Statistics (NBS) and we arbitrary approximate desired coverage for the first dose in Tanzania to be 90% while the second dose was 80% which is the proposed coverage by WHO.

Calculation of the total financial and economic cost for the HPV vaccination was done by finding the price of quadrivalent vaccine according to UNICEF price then, we considered the inflation rate effect from Tanzania NBS to obtain the current price. After obtaining the financial cost per fully immunized girl FIG we multiplied by the target population to get the estimated current total cost for HPV vaccination program in Tanzania. Quantitative data (e.g. coverage, computation of budget) were analyzed descriptively by Microsoft excel 2016. The Yonsei University Research Ethics Committee provided study approval.

All published documents were obtained from PubMedicine journal, while unpublished documents were found from the WHO website, HPV Information Centre as well as the websites of the ministry of health (MoH) of respective countries. Many studies were reviewed but only those who have specifically spoked about the lessons which were learned during the demonstration or in detail explain the HPV vaccine coverage were selected for this study.

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The involved articles for both qualitative and quantitative studies were chosen by consecutively examining the titles, abstracts, and then the full-text according to the PRISMA flow chart (See Figure 1). The references for the relevant articles were manually searched and included in the eligible studies.

We extracted document and transcript data to a standardized format developed for new vaccine introduction by Gavi. Topics included were; national policy and planning, linking with other interventions, service delivery, workforce, monitoring and evaluation, financial support, sustainability, and scale-up. According to GAVI, the strategic focus area is the proposed focusing area for the new vaccine project (Gavi The Vaccine Alliance 2017). These areas can be used to monitor the progress of the new vaccination program that is supported by Gavi.

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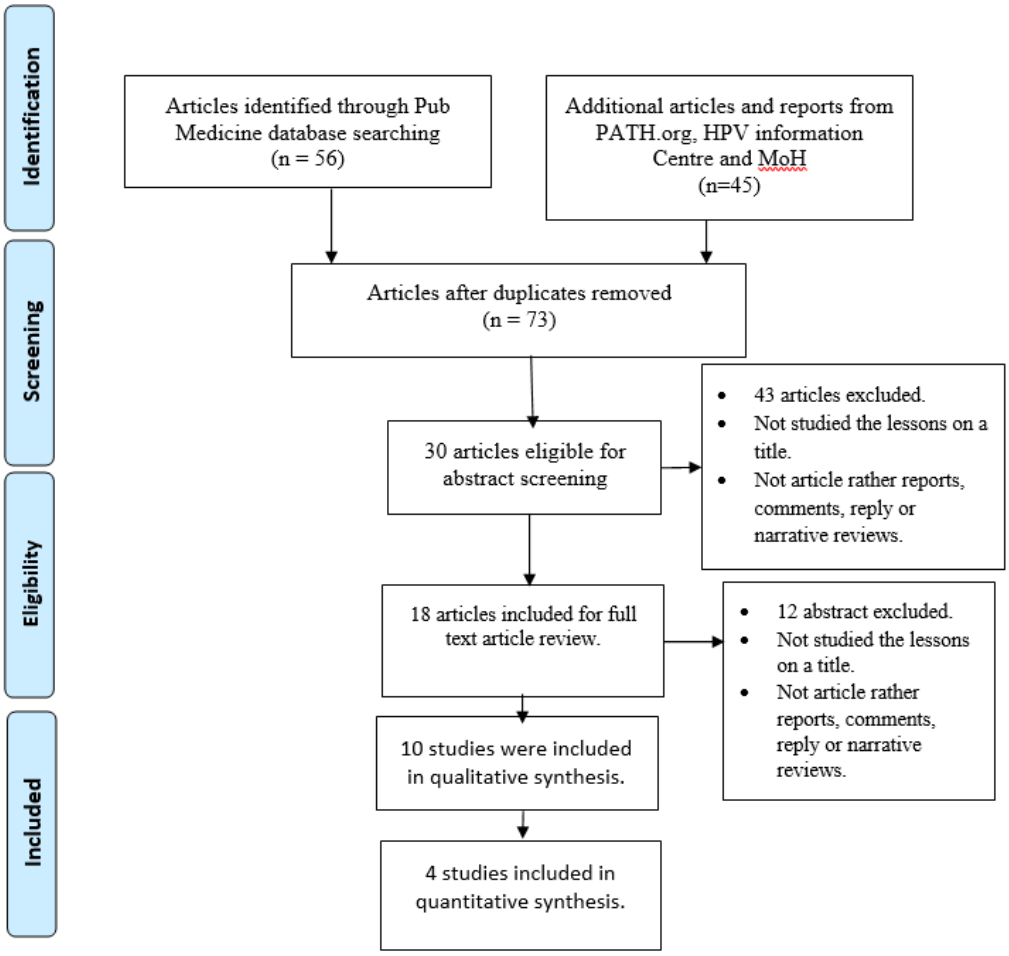
Figure 1: Literature search by PRISMA



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4. **RESULT**.

Data were gathered from 22 articles; 14 published articles from PubMed, 2 reports from PATH and HPV information center and 2 countries reports from a ministry of health of Uganda for the qualitative data while 4 published studies were obtained for quantitative data. Many studies were reviewed however failed to be involved in this study because they failed to elaborate as they specifically addressed a single lesson for the entire HPV vaccination program.

SSA region was divided into four main regions for the convenience of the study namely; East Africa (19 countries), West Africa (14 countries), Central Africa (08 countries) and South Africa (05 countries) which make a total of 46 countries (see Table 10. East Africa region had the highest proportion of countries with nation-wide HPV vaccination programs per region (42.1%), while the least was in Central Africa whereby among 8 countries none had a nation-wide HPV vaccination program. In West Africa, only 14.3% of the countries had a nation-wide HPV vaccination program while in South Africa about 40% of the countries in the region have nation-wide HPV vaccination programs.

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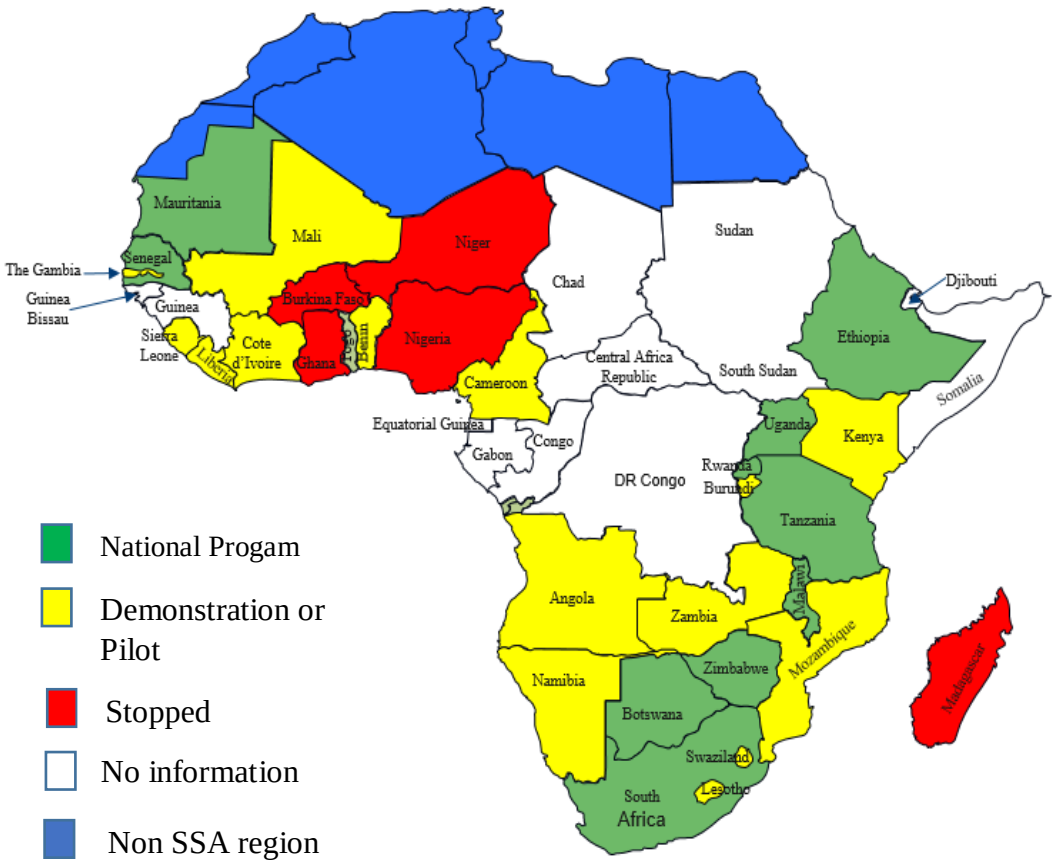
Figure 2: The map of SSA countries showing the HPV vaccination status



In general about 26.1% of SSA countries in the region already are having a nation-wide HPV vaccination program while most of remained are either on the demonstration phase or they have successfully completed the demonstration and are projected to start the nation-wide program. The remained are in the stopped phase which means, either the country was on

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demonstration or nation-wide HPV vaccination program but due to some reasons which will be discussed later; the program is currently stopped.

Table 1: Regions of sub-Saharan Africa with their HPV vaccination status quo.

	SSA sub-region				
	East Africa	West Africa	Central Africa	South Africa	Total
Number of countries	19	14	08	05	46
Nation-wide program *	08	02	0	02	12
Demonstration or Projected **	05	05	02	03	15
On-hold program *	01	05	0	0	06
No available information	05	02	06	0	13

**HPV information centre.org* ***PATH 2018*

12 SSA countries were found to have a nation-wide HPV immunization program by June 2019 (see Table 1), however, only 6 (60%) of them were involved in this review. 6 SSA countries with nation-wide HPV vaccination program were not involved in this program due to the unavailability of data, they include Lesotho, Mauritius, Senegal and Seychelles.

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4.1 Strategic focus areas

Table 2: Summary of lessons learned in 7 strategic focus areas in SSA

Specific Focus Area	Lesson
National Policy and Planning	Program flexibility
	Designated key community education messages.
	Evidence-based education to community.
	Adequate preparation.
	Government endorsement.
	Strong coordination.
	Ownership
Linkage with other interventions	Health workers and teachers play complementary roles.
	Active involvement of teachers.
Service delivery	School non-class based
	Mixed Strategy
	School class-based may involve an untargeted population.
	School class-based.
	Use the EPI system.
Workforce	Clearly defined roles of cadres involved
	Training.
	Use existing human resources.
Monitoring and Evaluation	Paper-based record is a barrier to real-time surveillance.
	Monitoring and Supportive supervision.
Financial support	Financial support may increase coverage
Sustainability and scale-up	Special attention to remote areas.
	Test for immunogenicity

The cardinal findings of this study had been enumerated in seven focus areas which are; national policy and planning, linking with other interventions, service delivery, workforce, monitoring and evaluation, financial support, sustainability and scale-up. All the lessons

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observed in these countries' HPV projects have been summarized in Table 2 in terms of ratio from the most frequent to the least frequent lesson.

The following table provides a summary of the countries which already have an HPV immunization program nation-wide (Mozambique is also in this table because it was involved in this study).

Table 3: The HPV Immunization Programs in SSA by June 2019.

Country	**Year of Introduction.**	**Delivery Platform.**	**Estimated Coverage.**	**Estimated drop-out rate.**
Botswana*	2015	School-based (grades 5–7) and out-of-school girls aged 9–13	-	5%
Ethiopia				
Lesotho*	2012	School-based	-	
Malawi	2019			5%
Mauritius*	2016	School based (grade 5)	-	-
Mozambique**	-	-	-	
Rwanda*	2011	School-based (grade 6) and out-of-school girls	HPV3 98.7% (2014)	
Senegal*	2016	School-based	-	

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Country	Year of Introduction.	Delivery Platform.	Estimated Coverage.	Estimated drop-out rate.
Seychelles*	2014	School-based (grade 6)	HPV1 77% HPV2 76% (2014)	
South Africa*	2014	School-based (grade 4)	HPV1 92% HPV2 72% (2014)	2.3%
Tanzania**	2018	School-based (grade 4) and out of school 14 years	HPV1 93% HPV2 92.6% HPV1 89% HPV2 78% (2016)	
Uganda*	2015	School-based (grade 4) and out-of-school girls aged 10	-	

**HumanPapillomavirusandRelatedDiseasesReport.Availablein:http://www.hpvcentre.net/statistics/reports/XFX.pdf (Accessed in November 02, 2019).*

***PATH.org (Accessed in October 20, 2019)*

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4.1.1 National policy and planning.

The area of the policy and planning is the vital determinant of the success or the failure of any project. Among 8 studies that were reviewed, 6(75%) have mentioned the importance of the policy and planning for the success of the HPV vaccination program. The lessons include; strong coordination, government endorsement, community ownership of the project, adequate preparation, adequate training and project flexibility.

Strong coordination and adequate preparation can be clearly be studied in Rwanda. Unlike many SSA countries, Rwanda did not undergo a demonstration project, even though it demonstrated the highest coverage among SSA which have national HPV vaccination according to the HPV information center statistics. In Rwanda there were multiple governmental and non-governmental department involved in the national program whereby the ministry of Health decided to widen its technical working group on vaccinations to include the Ministry of Education, the Ministry of Gender and Family Promotion, the Center for Treatment and Research on AIDS, Tuberculosis, Malaria, and other Epidemics, and health workers engaged in cancer care. Different responsibilities were assigned to these departments under the coordination of the ministry of health (Binagwaho et al. 2012).

In the demonstration project conducted in Uganda, it was reported that close coordination and adequate preparation by the health and education sectors lead to an effective community (PATH 2011). This is because the target population usually are girls who are either in schools

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or out of school within the community and therefore staffs from different ministry must come to work together for the success of the program.

Government endorsement was mentioned to be one of the key lessons learned in the demonstration of the HPV vaccine among SSA countries; 7 studies (87.5%) had reported. In the study conducted in Mozambique, it was evident that the HPV vaccine demonstration project implementation in all the sites was positively influenced by the engagement of Mozambique's first lady who identified cervical cancer as one of her legacy campaigns (Soi et al. 2018).

Community ownership and project flexibility were also important lessons mentioned in many articles that were reviewed. 6 (75%) of the studies reviewed proposed that when the community is highly involved in planning and implementing the demonstration project there are more chances of having a higher coverage. Also, these studies have proposed that the lower-level implementation units such as the district level should have the mandate of making changes in the main plan from ministry level to accommodate the specific need of the local community.

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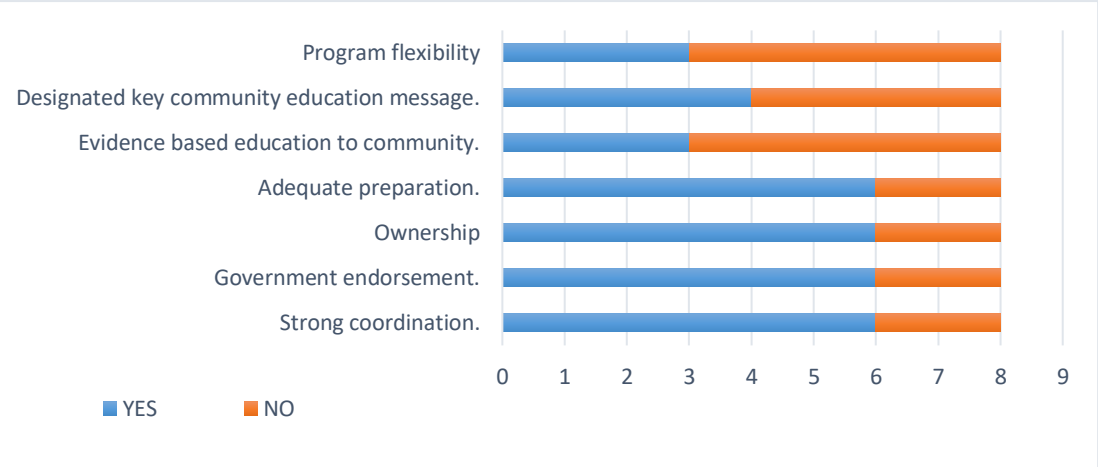
Figure 3: Significant Lessons learned in national policy and planning



Vertical line is a lesson learned and Horizontal line is the number of articles reviewed.

4.1.2 Linking with other interventions.

As the HPV vaccination is a multisectoral program many studies proposed linking the program with the ministry of education to increase coverage. Two important lessons that must be considered in linking with other interventions are; involvement of teachers and that health worker and teachers must play complementary roles.

In many studies, teachers had played many roles which are directly impacting the HPV vaccination. In the study conducted in Kwazulu Natal, SA teachers were the ones involved in monitoring the AEFI among vaccinee one week following vaccination. In addition, teachers set up meetings with the grade 4 and 5 learners to explain the project, and to obtain informed

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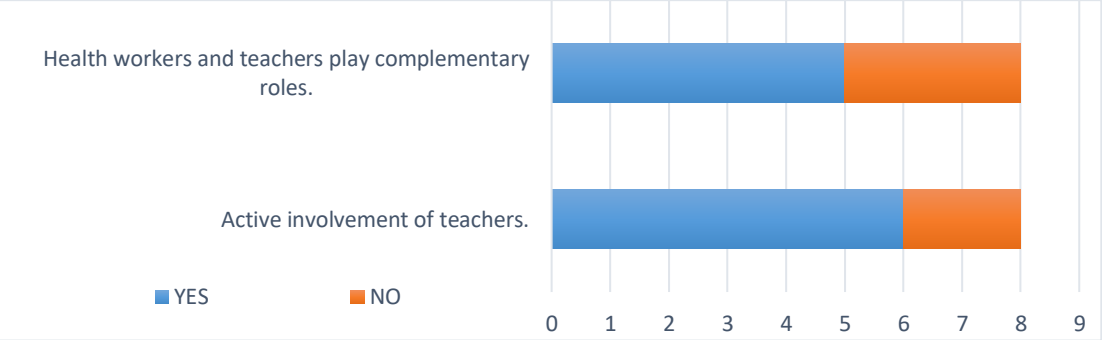
consent from parents, who received information leaflets, well in advance of the vaccination date (Moodley et al. 2013).

Also in this study, it was found that both teachers and health workers play a complementary role particularly in educating the community. In the study which was conducted in Uganda, health workers were the ones who trained the teachers about the importance of vaccination and in turn, the teachers who could easily reach the girls took the opportunity to train the girls and caregivers (PATH 2011).

In Tanzania during the demonstration project the vaccination schedules were planned by health workers in collaboration with school teachers and all activities were to be stipulated in the micro plan (GAVI 2017). The overall outcome of this collaboration between the teachers and health workers was increased coverage in which all the activities will be stipulated in.

Figure 4: Significant Lessons learned in Linking with other interventions



Vertical line is a lesson learned and Horizontal line is the number of articles reviewed.

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4.1.3 Service delivery.

Among 8 studies reviewed in this study; 3 articles proposed a school-based strategy can be used to achieve a high coverage, other 2 articles specifically mentioned a school class-based strategy can be used to achieve a higher vaccine coverage, also other 2 suggested that a mixed strategy which is both school-based and community or healthcare-based strategy can be used and 1 study specifically suggested school non-class based strategy.

The study which was conducted in Malawi showed that it was feasible and acceptable to administer HPV vaccine to adolescent girls using school class-based strategy in Malawi. High coverage of fully immunized (at least 2 doses) of 86.5%, 91.1% and 83.3% were achieved in year 1, 2 and 3, respectively and similar results were found in Tanzania (83.8%), Uganda (87.8%) and Rwanda (93.2%) (Msyamboza et al. 2017). However, providing an HPV vaccine in a class-based strategy has a disadvantage of involving young girls out of the targeted population as it has been shown in the study conducted in Malawi (Msyamboza et al. 2017).

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Figure 5: Significant Lessons learned in Service delivery

Vertical line is a lesson learned and Horizontal line is the number of articles reviewed.

4.1.4 Workforce.

Two most common learned lessons in the area of the workforce from articles review in this study including; the use of existing human resources and training. These two were proposed from 75% of all studies, moreover, one study has proposed having a clearly defined responsibility of each person involved in the program. Training should take place prior to the launching of the program and it should be organized for different participants of the vaccination program including the community.

Also, the use of the existing human resources both from the MoH and ministry of education was reported to be adequate by most of the studies. However, in a few studies it was proposed that; there might be a need to hire temporary personnel for mobilization of the community.

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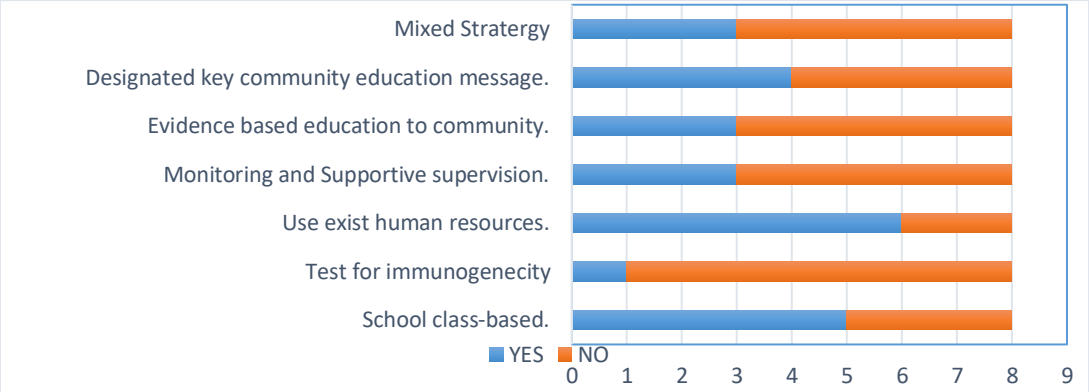
Figure 6: Significant Lessons learned in Workforce



Vertical line is a lesson learned and Horizontal line is the number of articles reviewed.

4.1.5 Monitoring and Evaluation.

Three studies of eight (37.5%) had mention lessons about monitoring and evaluation in this review. The two lessons are; to achieve higher coverage it is important to have monitoring and supportive supervision program of HPV vaccination and there is a need of having real-time surveillance instead of paper-based surveillance.

Monitoring and evaluation were mentioned to be an important tool for achieving higher immunization coverage in some few HPV demonstration projects in SSA. In Uganda it was reported that regular and targeted supervision visits by the Ministry of Health and district health teams helped make health providers feel more supported and accountable for performing key tasks, for example, supportive supervision involved helping health workers understand that

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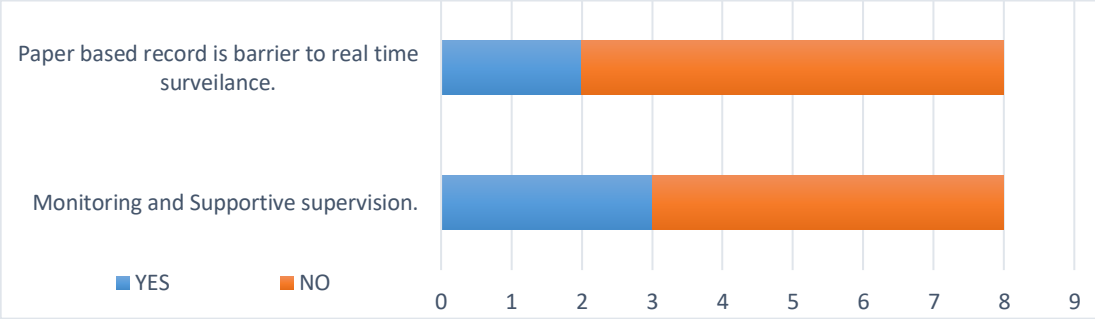
collection of accurate and complete data would be critical to planning subsequent vaccination activities (PATH 2011).

Also in the study held in Kwazulu Natal in SA, it was learned that there is a need of having real-time surveillance instead of paper-based surveillance. The paper proposed that to enable proper planning and finally the success of the program it was important to have an electronic monitoring tool that will enable to obtain real-time data (Moodley et al. 2013).

Figure 7: Significant Lessons learned in Monitoring and Evaluation



Vertical line is a lesson learned and Horizontal line is the number of articles reviewed.

4.1.6 Financial support.

The availability of financial resources can also contribute to the success of the HPV vaccination project. This was the lesson learned from one of the studies which were conducted in Mozambique whereby among the factors that contributed to the high performance of the district, availability of funds was mentioned.

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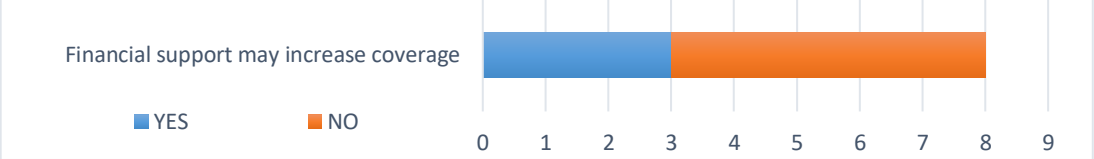
In this study, the health director of one district reported that the main challenge for the HPV project was insufficient funds which led to non-payment of the health workers and other participants that is teachers and community leaders' per diems (Soi et al. 2018).

Figure 8: Significant Lessons learned in Financial Support



Vertical line is a lesson learned and Horizontal line is the number of articles reviewed.

4.1.7 Sustainability and scale-up.

Two lessons were learned from different studies about scaling up of the HPV project in SSA countries. One is the importance of special consideration of the remote areas. Many of the SSA countries are characterized by remote places where it is relatively difficult to be reached. This area contains a considerable number of the target population who are to be vaccinated as well if the good coverage is to be met.

In harder-to-reach communities in Uganda, it was reported that efforts to educate and prepare the community in advance were inadequate; for example, where homes were located very far apart, local leaders were not provided with sufficient transport to reach them all, or roads were

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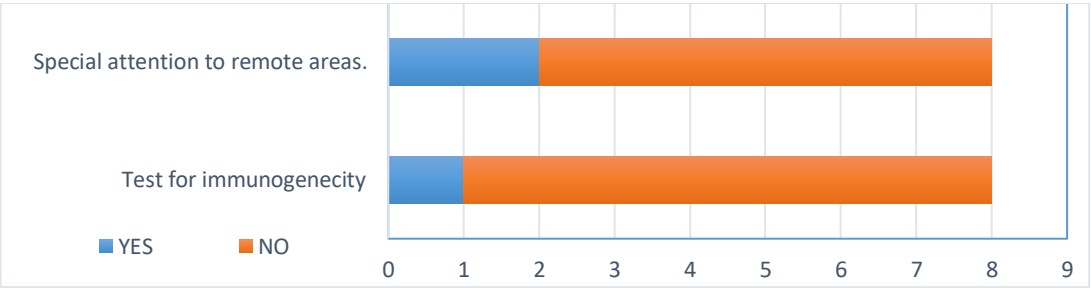
made impassable during the rainy season and this resulted to comparatively lower coverage as compare to central parts (PATH 2011).

In addition, one study recommends the test of immunogenicity among the sample of students who were vaccinated in the class-based. This was advocated in the study conducted in Malawi and the reason being, WHO recommends 2 doses for the girls between 9-14 years old, but in class-based some of the vaccinee maybe 8 years old and less or 15 and older. Therefore it was not clear that this group would be immunized against HPV vaccination or not (PATH 2011).

Figure 9: Significant Lessons learned in Sustainability and scale-up



Vertical line is a lesson learned and Horizontal line is the number of articles reviewed.

4.2 Comparison of the coverage of HPV vaccines by doses.

In this study, it was found that the coverage of the HPV vaccination usually tends to decrease from the first dose to the subsequent one. From all studies that were reviewed the percentage coverage drop from first dose through the third dose however there was a variation of degree

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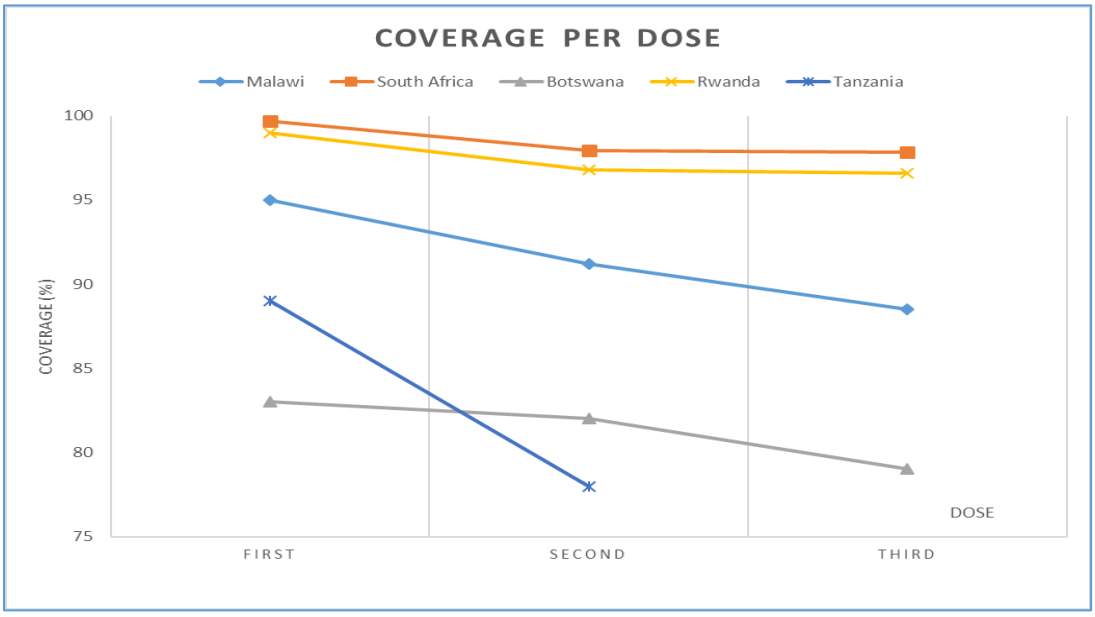
of dropping from study to another. The lowest variation of degree of dropping was found in the study which was conducted in Kwazulu Natal while the highest variation between doses was found in the study conducted in Malawi. Figure 11 shows the dose coverage in terms of percentage.

In the second year of the demonstration project, Tanzania had only two doses regimen which still ends up to have a comparable low coverage of 89% and 78% for dose 1 and 2 consecutively. Reasons for dropping the vaccination have been articulated on the next objective.

Figure 10: Comparison of the HPV vaccination coverage by doses in SSA countries.



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4.3 Reasons for partial or no vaccination

In many demonstration projects, it was found that the percentage coverage of the target population usually tends to decrease from the first dose to subsequent doses. Several reasons were identified among them school absence and parents' denial of consent were reported to be the most common cause of partial or no vaccination.

Others include; school drop-out, transferring to another school, limited allocated time to identify the girls, inconvenience of time for vaccination, pain at the injection site and uncleanness of the health facilities used for vaccination.

In one of the study conducted in Zomba district in Malawi transferring from one school to another contributed to about (50)76.9% of the schoolgirls who did not complete their vaccination and 7(10.8%) of the girls did not show up in vaccination due to school dropout (Msyamboza et al. 2017).

4.4 Budget impact of the single-dose regimen.

In this study, it was also found out that both financial and economic costs for HPV vaccination in Tanzania shall tend to increase. We estimated the financial price of the quadrivalent vaccine in Tanzania to be 2.92 USD in 2020 which is about 21.23% raise as compared to the financial price of the HPV vaccine in 2015. Base on the inflation rate of the country, this figure may keep rise. (See Table 3)

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Also, the economic cost for the HPV vaccine shall also increase from 10.08 USD to about 12.83 USD in 2020 which is equivalent to 21.43%. Although economic cost involves the purchasing cost which is usually covered by Gavi for most LMIC, there are other costs like vaccine delivery and cold chain that need to be covered by to country. Therefore the country needs to be prepared for these costs.

Table 4: Financial, Economic and total cost for HPV vaccine in Tanzania 2012 - 2020

Year	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Inflation rate (%)*	16%	7.90	6.10	5.60	5.20	5.30	3.50	5.14	5.14
Vaccine Financial cost ($)	1.73	2.01	2.17	2.30	2.43	2.55	2.69	2.78	2.92
Vaccine economical cost ($)	7.59	8.80	9.50	10.08	10.64	11.20	11.79	12.20	12.83
Total Vaccine price ($)	**9.32**	**10.81**	**11.67**	**12.38**	**13.07**	**13.75**	**14.48**	**14.99**	**15.76**

**Tanzania National Bureau of Statistics*

The total financial and economic cost for this study was obtained by multiply by the actual estimated target population which for the case of Tanzania is a girl aged 14 years old. According to Tanzanian NBS the population of the country is expected to grow by the rate of 3.1% a year up to 2013. We obtain the actual number of girls age 14 up to 2018 from NBS and then multiplied by 3,1% to estimate the target population in 2019 and 2020.

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Table 5: The total Financial, Economic cost and the Amount saved for the HPV vaccine from 2015 to 2020

Year	2015	2016	2017	2018	2019	2020
Target Population*	595,500	613,960	633,606	653,242	673,492	694,370
Cost per FIG (Financial) in USD	2.30	2.43	2.55	2.69	2.78	2.92
Cost per FIG (Economical) in USD	10.08	10.64	11.20	11.79	12.20	12.83
Total cost (Financial)	All in USD					
Dose 1	1,232,685.00	1,342,730.52	1,454,125.77	1581498.882	1685076.984	1,824,804.36
Dose 2	1,095,720.00	1,193,538.24	1,292,556.24	1405776.784	1497846.208	1622048.32
Total cost dose 1 & 2 (Financial)	2,328,405.00	2,536,268.76	2,746,682.01	2,987,275.666	3,182,923.192	3,446,852.68
Amount saved in single dose regimen (Financial)	**1,232,685.00**	**1,342,730.52**	**1,454,125.77**	**1,581,498.88**	**1,685,076.984**	**1,824,804.36**
Saved	**47.06%**	**47.06%**	**47.06%**	**47.06%**	**47.06%**	**47.06%**
Total cost (Economical)	All in USD					
Dose 1	5,402,376.00	5,879,280.96	6,386,748.48	6,931,550.86	7,394,942.16	8,017,890.39
Dose 2	4,802,112.00	5,226,027.52	5,677,109.76	6,161,378.54	6,573,281.92	7,127,013.68
Total cost dose 1 & 2 (Economical)	10,204,488.00	11,105,308.48	12,063,858.24	13,092,929.41	13,968,224.08	15,144,904.07
Amount saved in single dose regimen (Economic)	**2,746,682.01**	**5,226,027.52**	**5,677,109.76**	**6,161,378.54**	**6,573,281.92**	**7,127,013.68**
Saved	**47.06%**	**47.06%**	**47.06%**	**47.06%**	**47.06%**	**47.06%**

**Tanzania National Bureau of Statistics*

The results were; Tanzania will save about 7.1 million USD for the year 2020 alone as a economic and 1.7 million USD as financial cost if there shall be enough scientific evidence

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that a single dose regimen is as effective as the current two doses regimen, equivalent to about 47.06% of the entire budget for the HPV vaccination in the country. (See Table 4)

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5. **DISCUSSION**.

This is among studies conducted in SSA with a goal of recommending the plan on how to conduct an HPV vaccination program by studying the experience of HPV demonstration projects in SSA countries. Many articles had studied how to effectively conduct an HPV demonstration project in LMIC countries, however, in this study it was assumed that there are unique circumstances for the SSA region to be considered if HPV vaccination is to be successfully conducted. Also, this study had covered the budget impact analysis of a single dose regimen for HPV vaccination in Tanzania.

HPV vaccination project may be difficult to run owing to the unique target population as well as the need for multiple doses. It is crucial for some of the SSA countries which had not yet conducted the demonstration project or they have an ongoing program, to learn from other SSA countries that had successfully conducted their projects. Tanzania had launched a nationwide HPV immunization program in August 2018 however, there was a relatively low coverage achieved during the demonstration of the project, therefore Tanzania, as well as other SSA countries, can learn from this study to amend their program so as to improve the coverage of all doses. For convenience, this study had summarized the common practices in seven focus areas.

In the area of national policy and planning; this study found out that it is important to have adequate preparation before starting the program, community ownership of the project,

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governmental endorsement and strong coordination among different stakeholders participating in the vaccination program may provide a guide to an enormous acceptability of the HPV vaccination project in SSA countries.

These findings had collectively been reported in 6 of 8 of the studies that had been reviewed (75%). National policy and planning should cover activities such as identification of the target population, logistics such as vaccine delivery and cold chain, as well as assigning different roles for different workers. The HPV vaccination program has a uniqueness in the sense that its target population is a girl aged 9-14 years old girls (for most of LMIC). Similar approaches used for other vaccines delivery cannot provide significant coverage when applied, therefore it is important for implementers to have adequate preparation so as to locate the target population for maximum coverage.

Adequate preparation also means more time to design the program which usually involves two or more ministries that often do not work together. In many SSA countries, HPV vaccination programs are being conducted under the collaboration of MoH and the ministry of education. Adequate preparation will allow these governmental departments to come together to learn about their weaknesses and strengths and see how to adjust them so as to meet the intended goal.

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Adequate preparation has also been shown by Howard et al.2017 in the study to find what works for HPV vaccination in LMIC. The study mentioned that allowing sufficient time for planning and micro-planning as well as allow enough time for social mobilization. This collectively implicates that adequate time for preparation may increase the coverage.

It is equally important that the planning process involves the community so as to create the community ownership of the program. Community ownership of the program in this study can be defined as the state where the community (vaccinee, caregivers and other members of society) are the primary decision-makers on how the program should be conducted. When the community owns the project they can plan in the way that they can accommodate themselves in the program regardless of their busy schedule.

According to Soi et al.2018 in one of the study conducted in Mozambique to compare the determinants of the performance of HPV project among different districts it was found that vaccine delivery model, was designed at central MoH level to be primarily school-based, however the design did not consider nor address existing differences in proportion of girls enrolled in schools in the disparate demonstration districts, each of which presented a different socio-cultural and economic setting and therefore; it was suggested in the study that if the lower-level unit of implementation were allowed to adjust the plan based on the local need, it might have increased the vaccine coverage. Soi et al.2018 further explain that in some of the district there was low vaccination coverage as the community entirely depends on the Muslim

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leaders call imam for instruction on what to do. For imams were not involved during the planning, therefore most of Muslim vaccinees did not show up in vaccination.

Government endorsement of any program tends to improve the participation of the community, especially when the program is been co-implemented with the private sector. In this study, it was found that most in most of the countries where HPV demonstration projects were conducted, the community readily accepted the program if the official from the government or their family members were directly involved not only as the campaigners but also as the vaccinee 6 of 8 studies reported (75%).

Another important lesson was about strong coordination among the stakeholders. This was also reported among 6 of 8 studies that were reviewed. Usually strong coordination and governmental endorsement are the key responsibility of the government of a specific country and they support each other. As the HPV vaccination may involve many governmental and non-governmental stakeholders it becomes important to have strong coordination to organize all activities without causing overlapping of duties. In Rwanda, this was evident as the government played a key role in organizing all stakeholders who participated in the program (Binagwaho et al. 2012).

Other lessons in the area of national policy and planning which for in few studies but with huge impact in that setting include; having a designated key community education message

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during the HPV vaccination training and sensitization. This will enable all people to have one clear message and therefore reduce the contradictions and confusion. In the study which was conducted in Uganda, it was insisted to have a clear message about HPV immunization.

According to PATH, in demonstration project report in Uganda, respondents appreciated that the language in the materials was simple and the pictures were clear and understandable also teachers and community leaders felt that they made it easier to explain to others about cervical cancer and the need for vaccination to prevent HPV infection.

In the area of linking with other interventions, two lessons were identified one being; active involvement of teachers reported in 6 of 8 studies (75%) and the second is health workers and teachers play complementary roles reported in 5 of 8 studies (62.5%). In all 8 studies, MoH worked with the ministry of education to meet the intended goal. In some countries such as Rwanda, the studies have clearly mentioned the ministry of finance as another important stakeholder for the HPV vaccination program, while other studies did not clearly mention the ministry of finance.

Active involvement of teachers and complementary role-playing between healthcare workers and teachers are the key strategies to achieve high HPV vaccine coverage. This is often the case when a school-based vaccination delivery strategy is used. Usually, teachers are used to identify the target population and in some areas, they collect data following the vaccination.

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In the study that was conducted in KwaZulu Natal SA, it was reported that awareness, information and education sessions on cervical cancer, screening and the HPV demonstration project were conducted with school principals, governing bodies and teachers. Thereafter, teachers set up meetings with the grade 4 and 5 learners to explain the project, and to obtain informed consent from parents, who received information leaflets. (Moodley et al. 2013).

Service delivery strategy also plays a critical role to meet the targeted population. Mainly there are three methods that were proposed at different frequencies from the review. They included; the school class-based, school non-class based and mixed strategy. 5 of 8 studies (62.5%) suggested the used of the school class-based, while 3 of 8 (37.8%) proposed a mixed strategy that combined both a school-based and community-based delivery approach. Only 1 study proposed a school non-class based delivery strategy.

This scattered result was also reported by Howard et al. 2017, in this article it was explained that different strategy mixes (e.g. schools, health facilities, and outreach) could work in different contexts within the same country, as logistics and school enrolment were not homogeneous across each country.

Moreover in the study that was conducted in Uganda mentioned that whenever a school class-based strategy is used it may lead to vaccinating the untargeted population as the selection of target population base on class may introduce the student whose age is out of WHO-

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recommended age (9-14). This raises the question of the need for tests of immunogenicity to the vaccinee who was vaccinated by a school class-based strategy.

In the area of workforce, two strong lessons were found which are training and the use of existing human resources. These two lessons were suggested by 75% of the studies which were reviewed. 6 of 8 studies recommended that there was no need to hiring a new workforce for the HPV vaccination program instead, the existing human resource can be adequate to run the program.

In the demonstration project report of Tanzania held between 2016 to 2017, it was reported that no additional personnel is needed as existing health workers and school teachers will be used to deliver the services in schools, what was expected was only to increase the number of outreaches (GAVI 2017).

Training appeared the most important determinant of coverage when comes to the area of the workforce. All articles that address the importance of the training specifically mentioned that thorough training is one of the most important perpetuators of good vaccine coverage. Training should be considered in two main groups of immunization program participants.

The first area of the training involves the immunization workforce, this range from healthcare workers, teachers and all other parastatal workforces that are going to be involved in the immunization program. The second side was training the community particularly the

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caregivers. In most of the study, the vaccinee would receive a vaccine only if the parent or the caregiver had signed a consent form. To do that it was important for the caregiver to be trained and understand the importance of the vaccination. In the study conducted in KwaZulu Natal, it was recommended that the 'use of simple visual materials, in the appropriate language(s), should be used for training community' (Moodley et al. 2013).

Having a clearly defined responsibility of each person involved in the program was also reported to be one of the lessons learned in one study conducted in Mozambique. In NIP of many countries, the roles of non-healthcare personnel are not defined therefore a new way must be found on how to collaborate with teachers and other community leaders (Soi et al. 2018).

This was suggested so as to reduce the interference of duties in the complex vaccination program like HPV. The author documented that, while it may not be possible to eliminate complexity due to HPV's novel target group (pre-teen girls) with no established health services in most countries, complexity could be minimized by clearly defining how health workers collaborate with teachers and community leaders during campaigns (Soi et al. 2018).

Monitoring and evaluation was another focus area in which few studies mentioned. Two lessons were learned about in this SFA and they include monitoring and supportive supervision program of HPV vaccination and there is a need of having real-time surveillance instead of paper-based surveillance.

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Among eight studies, only three studies (37.5%) of the studies clearly mentioned that monitoring and supportive supervision program are important for the success of the program. These include the studies conducted in Mozambique, Malawi and South Africa. Frequent monitoring and supervision by the key player always enable the lower level implementers to feel more supported but also it provides them with the opportunity to learn and adjust their shortcomings during the program as it was reported by PATH in the HPV demonstration project in Uganda.

Also in Uganda, it was proposed that for better results of the project it is important to stop using paper-based surveillance and shift to real-time surveillance. This shall help to respond easily to the needs of the program once it happens. But also the use of paper exposes the data to a wide range of risks which can be avoided when the electronic applications are being used.

Financial support for incentives of immunization workers was also been identified as one of the lessons to achieve high HPV coverage. Most of the LMIC in SSA receive financial support from Gavi for purchasing the vaccine and a fraction of the financial cost to run the program. However, most of the financial cost is to be covered by the government of the respective countries. Apart from the support to purchase the vaccine the study by Soi et al.2018 reported extra financial support. In this study, there were some districts in which Gavi supported funds for incentives for the workers who participated in the program while other districts did not receive any incentive. Finally, it was found that HPV vaccination coverage of eligible girls in

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the government-funded districts, where incentives were not paid, was much lower than the coverage reported in the high performing district, where financial support from Gavi ensured that all individuals supporting the HPV project implementation received incentives. Therefore for those countries like Tanzania and Botswana where there is reported lower coverage during demonstration projects can pilot the incentivizing program to improve the coverage of the vaccine.

The area of sustainability and scaling-up had two lessons which included; focus on the remote areas and test of the immunogenicity. Both lessons were reported from a similar study conducted in Uganda. Usually the remote and hard to reach places are left behind in most of the program. It was therefore reported to cover more girls in the immunization program in SSA countries where infrastructure is still a question it is important to consider the remote areas.

The test of immunogenicity was also raised in Uganda where the vaccination by the school class-based approach was used and the doubt of vaccination the girls out of WHO-recommended age (9-14) came up. Therefore as identify the target population by their age could be difficult and therefore the class-based strategy is used, it is also important to bear in mind the age limit and if there is reasonable doubt on whether the vaccinee had acquired an immunity or not then the test for immunogenicity can be conducted.

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In this study, we also compared the coverage of the HPV vaccines by doses. As has been shown in many studies; the coverage of doses usually tends to decrease from the first dose to the subsequent one; this study had also compared the coverage by doses from four SSA countries which are Botswana, Rwanda, South Africa and Tanzania. As many African were conducting a three doses HPV vaccination program; so all countries we compared three doses except for Tanzania and it was found that South Africa and Rwanda were having comparatively higher coverage for all doses as compared to Botswana and Tanzania.

Rwanda had 99%, 96.8 and 96.6% for dose 1, dose 2 and dose 3 respectively owing to several reasons include; government ownership and support, good communication and adequate preparation. Similar factors were observed in South Arica which had slightly higher coverages of 99.7%, 97.9% and 97.8% coverage for dose 1, dose 2 and dose 3 respectively. Some of these factors have already been seen as important lessons for some SSA countries to achieve high HPV vaccination coverage.

According to Vermandere et al. 2015, the government of Rwanda took full responsibility for the entire program and coordinated all stakeholders in the HPV vaccination program. The government also managed to pursue Merck Company to have a free vaccine for three consecutive years and the vaccines at the concessional price on the continuing years. Involvement of the government for improving the coverage was also mentioned in the study

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conducted in Kenya whereby, most participant claims the presence of the government on the program reassure them about the safety of the vaccine (Watson-Jones et al. 2015).

Good communication was also highlighted in the study which was conducted in KwaZulu Natal SA whereby mass media communication was advocated to be the answer for spreading the desired message to the community. Mass media, especially local radio stations, should be used to disseminate information about the HPV vaccine, to raise awareness and reinforce key messages (Moodley et al. 2013).

Despite a high reported dropping out rate in some HPV vaccination programs such as in Botswana and Tanzania (both about 5%); most of the studies were found not to elaborate the factors that had increased a dropout rate. Only three studies conducted in Tanzania, Uganda and Malawi explain some of the reasons resulted in partial or no vaccination whereby absence and parents' denial of consent were found to be the leading factors.

In one study conducted in Tanzania to determine the reason of receiving or not receiving HPV vaccination it was found that; 85 (53%) of 159 cases did not receive dose 1 of vaccine because the pupil was absent from school on the vaccination day, 70 (44%) because a parent refused, 2 (1%) because the girl refused and 2 (1%) for other reasons (Watson-Jones et al. 2012).

The parents denied to provide the consent for their children vaccination for several reasons includes; low awareness of the risk of cancer of the cervix among girls whereby Watson-Jones

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et al reported that there was a large proportion of the parents who did not have education about the advantage of HPV vaccine to their girls. In one study conducted in Tanzania to determine the reason of receiving or not receiving HPV vaccination it was found that; 85 (53%) of 159 cases did not receive dose 1 of vaccine because the pupil was absent from school on the vaccination day, 70 (44%) because a parent refused, 2 (1%) because the girl refused and 2 (1%) for other reasons (Watson-Jones et al. 2012).

The parents denied to provide the consent for their children vaccination for several reasons includes; low awareness of the risk of cancer of the cervix among girls whereby Watson-Jones et al.2014 reported that there was a large proportion of the parents who did not have education about the advantage of HPV vaccine to their girls. Also in one study conducted in Kenya several factors statistically significant were found to cause partial or no vaccination and these include low knowledge of HPV and the single male guardian (Mabeya et al. 2018).

On the budget impact analysis for a single dose regimen of HPV vaccination, we used both financial and economic cost to approximate the cost that can be saved by the government of Tanzania when it moves to a single dose of HPV vaccination. It is clearly known that currently WHO recommends a two doses regimen for HPV Vaccination however, many studies are currently being carried to support the effectiveness of a single dose for HPV vaccination.

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A single dose regimen for HPV vaccination may have multiple benefits for the country as it may increase the coverage fo full immunized girl as it was reported in this study that the first dose tends to have higher coverage compare to subsequent doses, but also it may reduce the overall running cost for the HPV vaccination program. As Tanzania qualifies for Gavi's support, it receives free vaccines hence the cost of purchasing vaccines was included in financial cost. Moreover, when Tanzania and other LMIC graduates from Gavi's NVS, they shall entirely rely on the government's budget to purchase the vaccines and therefore knowing how single dose can reduce the budget burden may help the planners to make an informed decision.

We estimated that Tanzania would save about 5,927,820.57 USD on an average from the year 2015 to 2020 as an economic cost. Moreover, in the year 2020 alone, Tanzania can save about 7,127,013.68 USD as an economic cost. In this study, the economic cost has been showing to increase per annum and we expect that this economic cost shall continue to rise from year to year and therefore countries shall pay more for vaccines.

Tanzania and other SSA countries that still depend on Gavi support for the HPV vaccination program can shift to a single dose regimen to improve the coverage as well to reduce the cost of running the program once the effectiveness of the single-dose has been scientifically established. To do that we recommend further studies in this area of the effectiveness of the single-dose regimen of the HPV vaccination. The trend of HPV vaccination started with three

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doses, with the first two doses being one month apart and the third dose being six months apart. Currently WHO recommends two doses of HPV vaccine at least six months apart. More researches can establish the effectiveness of the single-dose regimen of HPV vaccine and help LMIC to sustain the programs after graduating from Gavi's assistance but also this shall help to increase the overall vaccine coverage.

Another area that we recommend for future studies is "the factors contributing the acceptance of HPV vaccine among girls caretakers in SSA". As it has been reported by Watson-Jones et al.2014 that parents and caretakers' denial for consenting girls' vaccination contributed to the coverage; it is therefore important to identify factors that determine the acceptability of the parents and caretakers' consent to girls vaccination.

This study also faces several limitations include; failing to include all SSA countries that have nation-wide HPV vaccination programs or had successfully conducted their demonstration projects as mentioned in the inclusion criteria. This is due to the two reasons; one being the availability of the vaccine that will completely prevent the HPV infection and two; a scientifically established relationship between the HPV and the cancer of the cervix and other cancer. Also in the budget impact analysis, the study used the unstratified secondary data for the financial and economic cost of HPV vaccination in Tanzania which hide the actual cost of HPV vaccination in the country.

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6. CONCLUSION.

Most of the lessons learned were reproducible for many countries and they were supported by other articles that were not reviewed in this study. The highest consistency in the lessons was found in the area of national policy and planning. Also, many SSA which are currently conducting the nation-wide program had reported a significant low coverage of the targeted population.

It is there important for SSA countries which ad reported a low HPV vaccine coverage to translate their program into a new project by following the best practice of those SSA countries which had reported a significantly higher coverage as this study revealed that there are similar lessons among SSA countries.

In addition, a single dose regimen for HPV vaccination has proved to reduce some budget burden by reducing the financial and economic cost in Tanzania, once WHO has recommended a single dose regimen it is important for SSA countries to move to a single dose HPV vaccination. Apart from being the second commonest cancer among women worldwide, more efforts should be directed to the reduction of the HPV infection and ultimately the cancer of cervix.

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REFERENCES.

1. Binagwaho, A., C. M. Wagner, M. Gatera, C. Karema, C. T. Nutt, and F. Ngabo. 2012. 'Achieving high coverage in Rwanda's national human papillomavirus vaccination programme', *Bull World Health Organ*, 90: 623-8.
2. Chido-Amajuoyi, O. G., J. F. Domgue, C. Obi-Jeff, K. Schmeler, and S. Shete. 2019. 'A call for the introduction of gender-neutral HPV vaccination to national immunisation programmes in Africa', *Lancet Glob Health*, 7: e20-e21.
3. GAVI. 2017. 'Application Form for Gavi NVS support Submitted by The Government of United Republic of Tanzania'. https://www.gavi.org/country/tanzania/documents/.
4. GAVI. 2019. 'Eligibility for Gavi support is determined by countries' national income.', Accessed 11/10/2019. https://www.gavi.org/support/sustainability/eligibility/.
5. Gavi The Vaccine Alliance. 2017. 'Strategic focus areas'. https://www.gavi.org/support/pef/strategic-focus-areas/.
6. Howard, N., K. E. Gallagher, S. Mounier-Jack, H. E. D. Burchett, S. Kabakama, D. S. LaMontagne, and D. Watson-Jones. 2017. 'What works for human papillomavirus vaccine introduction in low and middle-income countries?', *Papillomavirus Res*, 4: 22-25.
7. HPV information centre. 2019. 'Human Papillomavirus and Related Diseases Report'. https://hpvcentre.net/statistics/reports/XFX.pdf?t=1571754734720.

연세대학교
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8. Ladner, J., M. H. Besson, M. Rodrigues, E. Audureau, and J. Saba. 2014. 'Performance of 21 HPV vaccination programs implemented in low and middle-income countries, 2009-2013', *BMC Public Health*, 14: 670.
9. LaMontagne, D. S., P. J. N. Bloem, J. M. L. Brotherton, K. E. Gallagher, O. Badiane, and C. Ndiaye. 2017. 'Progress in HPV vaccination in low- and lower-middle-income countries', *Int J Gynaecol Obstet*, 138 Suppl 1: 7-14.
10. Mabeya, H., S. Menon, S. Weyers, V. Naanyu, E. Mwaliko, E. Kirop, O. Orango, H. Vermandere, and D. Vanden Broeck. 2018. 'Uptake of three doses of HPV vaccine by primary school girls in Eldoret, Kenya; a prospective cohort study in a malaria endemic setting', *BMC Cancer*, 18: 557.
11. Markowitz, L. E., J. Gee, H. Chesson, and S. Stokley. 2018. 'Ten Years of Human Papillomavirus Vaccination in the United States', *Acad Pediatr*, 18: S3-s10.
12. Mboumba Bouassa, R. S., T. Prazuck, T. Lethu, J. F. Meye, and L. Belec. 2017. 'Cervical cancer in sub-Saharan Africa: an emerging and preventable disease associated with oncogenic human papillomavirus', *Med Sante Trop*, 27: 16-22.
13. Moodley, I., N. Tathiah, V. Mubaiwa, and L. Denny. 2013. 'High uptake of Gardasil vaccine among 9 - 12-year-old schoolgirls participating in an HPV vaccination demonstration project in KwaZulu-Natal, South Africa', *S Afr Med J*, 103: 318-21.
14. Msyamboza, K. P., B. M. Mwagomba, M. Valle, H. Chiumia, and T. Phiri. 2017. 'Implementation of a human papillomavirus vaccination demonstration project in Malawi: successes and challenges', *BMC Public Health*, 17: 599.
15. Panatto, Donatella, Daniela Amicizia, Cecilia Trucchi, Francesca Casabona, Piero Luigi Lai, Paolo Bonanni, Sara Boccalini, Angela Bechini, Emilia Tiscione, Carla Maria Zotti, Rosa Cristina Coppola, Giuseppina Masia, Angelo Meloni, Paolo

연세대학교
YONSEI UNIVERSITY

Castiglia, Andrea Piana, and Roberto Gasparini. 2012. 'Sexual behaviour and risk factors for the acquisition of human papillomavirus infections in young people in Italy: suggestions for future vaccination policies', *BMC Public Health*, 12: 623.

16. PATH. 2011. 'HPV Vaccination in Africa lessons learned from a pilot program in Uganda'. https://path.azureedge.net/media/documents/RH_hpv_lessons_learned_uganda_es.pdf.
17. Rodriguez, A. C., M. Schiffman, R. Herrero, S. Wacholder, A. Hildesheim, P. E. Castle, D. Solomon, and R. Burk. 2008. 'Rapid clearance of human papillomavirus and implications for clinical focus on persistent infections', *J Natl Cancer Inst*, 100: 513-7.
18. Schiffman, M., P. E. Castle, J. Jeronimo, A. C. Rodriguez, and S. Wacholder. 2007. 'Human papillomavirus and cervical cancer', *Lancet*, 370: 890-907.
19. Shiels, M. S., A. R. Kreimer, A. E. Coghill, T. M. Darragh, and S. S. Devesa. 2015. 'Anal Cancer Incidence in the United States, 1977-2011: Distinct Patterns by Histology and Behavior', *Cancer Epidemiol Biomarkers Prev*, 24: 1548-56.
20. Soi, C., S. Gimbel, B. Chilundo, V. Muchanga, L. Matsinhe, and K. Sherr. 2018. 'Human papillomavirus vaccine delivery in Mozambique: identification of implementation performance drivers using the Consolidated Framework for Implementation Research (CFIR)', *Implement Sci*, 13: 151.
21. The U.S. Food and Drug Administration. 2018. 'FDA approves expanded use of Gardasil 9 to include individuals 27 through 45 years old'.

연세대학교
YONSEI UNIVERSITY

https://www.fda.gov/news-events/press-announcements/fda-approves-expanded-use-gardasil-9-include-individuals-27-through-45-years-old.

22. Watson-Jones, D., N. Mugo, S. Lees, M. Mathai, S. Vusha, G. Ndirangu, and D. A. Ross. 2015. 'Access and Attitudes to HPV Vaccination amongst Hard-To-Reach Populations in Kenya', *PLoS One*, 10: e0123701.
23. Watson-Jones, D., K. Tomlin, P. Remes, K. Baisley, R. Ponsiano, S. Soteli, S. de Sanjose, J. Changalucha, S. Kapiga, and R. J. Hayes. 2012. 'Reasons for receiving or not receiving HPV vaccination in primary schoolgirls in Tanzania: a case control study', *PLoS One*, 7: e45231.
24. World Cancer Research Fund. 2019. 'Cervical cancer is the eighth most common cancer worldwide'. https://www.wcrf.org/dietandcancer/cancer-trends/cervical-cancer-statistics.
25. World Health Organization. 2019. 'Ten threats to global health in 2019'. https://www.who.int/emergencies/en/.